

Non-Technical Abstract

Cystic fibrosis (CF) is an inherited disease that affects 1:2500 live Caucasian births. Cystic fibrosis is caused by a defect in a single gene, the cystic fibrosis transmembrane conductance regulator (CFTR). The disease manifests clinically in the lung, intestinal and reproductive tracts, pancreas, and liver. The major cause of death results from mucous obstructions in the respiratory tract which lead to recurring bacterial infections and, eventually, respiratory failure. There is currently no effective cure for cystic fibrosis. Treatment of cystic fibrosis is directed at managing the symptoms and complications of the disease and consists of antibiotic therapy for the bacterial infections, physiotherapy to help remove the thick mucous, pancreatic enzyme replacement, nutritional support, and, more recently, DNase to reduce sputum thickness. In spite of the introduction of new treatments and more aggressive management of the disease, more than 90% of CF patients die of lung disease by age 30.

The CFTR gene encodes a protein that forms a channel in cell membranes. This channel regulates the balance of salts and water in cells. In CF patients, this balance is disrupted resulting in the clinical manifestations of the disease. Laboratory experiments have shown that a copy of the CFTR gene can be introduced into cultured cells isolated from CF patients or into mouse models of CF to correct this defect. The fact that CF results from defects in a single gene makes this disease an attractive candidate for gene therapy. Introduction and expression of a normal copy of the CFTR gene into the cells of CF patients may allow some correction of the imbalances caused by mutations in the CFTR gene.

GR213487B is a DNA-lipid complex composed of a plasmid, pMB113, that carries the human CFTR gene, and of cationic liposomes. The liposomes will deliver the plasmid DNA to cells following intranasal administration to CF patients. The purpose of this first proposed study is to determine if GR213487B is safe for patients. In addition, this study will collect information to determine if administration of GR213487B could potentially help CF patients by introducing a normal copy of the CFTR gene into cells.